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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/531,347	02/27/2006	Jost Seibler	100725-47 (KGB)	3093

27384 7590 10/01/2009

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EXAMINER	
NOBLE, MARCIA STEPHENS	
ART UNIT	**PAPER NUMBER**
1632	
MAIL DATE	**DELIVERY MODE**
10/01/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/531,347	SEIBLER ET AL.	
	Examiner	Art Unit	
	MARCIA S. NOBLE	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 July 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14-40,45,47 and 48* is/are pending in the application.

4a) Of the above claim(s) *14-40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *45,47 and 48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15 April 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/1/2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 7/28/2009 has been entered.

Status of Claims

Claims 14-40, 45, 47 and 48 are pending. Claims 14-40 were previously withdrawn as non-elected subject matter, as set forth in the Office Action, mailed 8/6/2008 (see page 2). Claims 45, 47, and 48 are amended and claim 46 is canceled by the response filed 7/28/2009. Claims 45, 47, and 48 are under consideration.

Withdrawn Rejections and Response to Arguments

The rejection of claims 45-47, under 35 U.S.C. 112, first paragraph, as set forth in the Office Action, mailed 4/28/2009 (pp. 3-9), because the specification, while being enabling for a **mouse** having stably integrated an expression vector comprising a shRNA construct under control of a ubiquitous promoter at a polymerase II dependent locus of the mouse genome by homologous recombination, wherein expression of said shRNA results in repression of expression of a gene targeted by said shRNA in said

mouse, does not reasonably provide enablement for 1) a rodent other than a mouse having stably integrated said expression vector into a polymerase II dependent locus, and 2) a transgenic rodent with no phenotype, is withdrawn.

Applicant's arguments, see page 8, par 5, filed 7/28/2009, with respect to scope of enablement rejection have been fully considered and are persuasive. Applicant asserts that the claims have been amended to recite "a mouse" and "wherein expression of said shRNA results in repression of expression of a gene targeted by said shRNA in said mouse". Applicant asserts that these amendments narrow the scope to claims to encompass the previously identified enabled subject matter in the scope of enablement rejection. These amendments and arguments are found persuasive. Therefore, the rejection of claims 45-47 under 35 U.S.C. 112, 2nd paragraph has been withdrawn.

The provisional rejection of claims 45-48, on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 27 and 30 of amended claims filed 5/30/2008 in copending Application No. 10/685,837, as set forth in the Office Action, mailed 4/28/2009 (pages 9-11), is withdrawn.

Applicant's arguments (see page 8, last par, filed 7/28/2009), with respect to obviousness-type double patenting rejection have been fully considered and are persuasive. Applicant filed a terminal disclaimer to address this rejection. The terminal disclaimer was approved on 9/4/2009. Thus, the obviousness-type double patenting rejection is withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 45 and 47 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 45 and 47 recite the limitation "said short hairpin RNA" in the last line of the claims. There is insufficient antecedent basis for this limitation in the claim. The preceding disclosures in the claims recite “a short hairpin RNA construct” and “said short hairpin RNA construct”, not "a short hairpin RNA". Therefore, there is insufficient antecedent basis for the recitation, "said short hairpin RNA".

Claim 47 is drawn to a tissue or cell culture obtained from a mouse. Claim 47 further recites, “wherein expression of said short hairpin RNA construct results in repression of expression of a gene targeted by said short hairpin RNA in said mouse”. This “wherein” clause is indefinite because it is inconsistent with the rest of the claimed subject matter. The claim is drawn to a tissue or cell culture and not a mouse. However, the “wherein” clause is drawn to a result that occurs in the mouse and not in the claimed tissue or cell culture. Therefore, it is not apparent how the “wherein” clause is intended to further limit the claimed tissue or cell culture because the “wherein” clause refers to a result in the mouse and not the claimed tissue or cell culture. For purposes of art consideration, the “wherein” clause is being interpreted as

encompassing a tissue or cell culture wherein expression of the shRNA construct results in repression of expression of a gene targeted by the shRNA construct in said cells of the tissue or cell culture.

Claim Rejections - 35 USC § 102/103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 45, 47, and 48 are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Lowe (Lowe et al. US 2008/0226553 A1; Pub Date:9/18/2008; effective filing date:9/27/2002).

Claim 48 is drawn to an expression vector comprising a short hairpin RNA (shRNA) construct under control of a ubiquitous promoter and sequences suitable for targeted integration at a polymerase II dependent locus of a mouse. Lowe discloses an

expression vector encoding a firefly luciferase shRNA construct flanked by two targeting sequences that target integration of the expression vector to the polymerase II dependent, *hprt* gene locus of a mouse genome. Upon recombination and integration of the expression vector into the *hprt* gene locus, the luciferase shRNA construct is operably linked to the ubiquitous mouse *hprt* promoter (Figure 23). Thus, the shRNA construct is under control of a ubiquitous promoter as claimed. Lowe discloses that this expression vector is intended for introduction into mouse embryonic stem (ES) cells (p. 17, par [0172], line 1 to par [0173], line 9). Thus, Lowe clearly discloses all of the limitations of expression vector as claimed.

Claim 47 is drawn to a mouse tissue or mouse cell culture comprising cells having an shRNA construct under control of a ubiquitous promoter and sequences suitable for targeted integration at a polymerase II dependent locus, wherein expression of said shRNA construct results in repression of expression of a gene targeted by said shRNA. Lowe discloses introducing the luciferase shRNA expression vector, discussed above, into cultured mouse ES cells comprising and expressing a firefly luciferase gene. Lowe further discloses that said introduction of the luciferase shRNA expression vector results in high levels of site specific integration of the expression vector into the *hprt* gene of the mouse ES cells (p. 17, par [0173], lines 1-9). Lowe discloses that expression of the luciferase shRNA expression construct by the mouse ES cells effectively suppressed firefly luciferase activity in the ES cells (p. 17, [0174], lines 1-10). The preamble of claim 47 recites a tissue or cell culture “obtained from a mouse”. The breadth of this recitation encompasses a product-by-process claim that encompasses a

tissue or cell product produced by the process of isolating tissues or cells from a mouse that harbors the claimed shRNA expression construct. While Lowe obtains the ES cell culture harboring the claimed expression vector by a different process (i.e.-directly introducing the expression vector into cultured ES cells), the ES cells disclosed by Lowe are structurally indistinguishable from the cells encompassed by the claims. Therefore, the recitation, "obtained from a mouse" in this instant does not impart patentable weight because the structural limitations of the claimed cell culture or tissue has been disclosed by Lowe. Therefore, Lowe clearly anticipates the claimed cell culture because Lowe discloses all of the structural limitations of the claimed cell culture.

Claim 45 is drawn to a mouse comprising an expression vector stably integrated by site specific integration at a polymerase II dependent locus, said expression vector comprising an shRNA construct controlled by a ubiquitous promoter and sequences suitable for targeted integration into the polymerase II depend locus, wherein expression of the shRNA construct results in repression of expression of a gene targeted by said shRNA in said mouse.

Lowe discloses that the shRNA expression construct and ES cells comprising the shRNA expression construct, as discussed above, are part of a system for creating genetically defined RNAi "epi-alleles" in mice using Cre-mediated recombination to stably integrate a single RNAi expression cassette into a single locus in the mouse genome. Lowe discloses that this technique will minimize clonal variation due to random integration events. Lowe discloses that the system was developed to mediate the integration of a single shRNA expression cassette into mouse ES cells. Lowe

discloses the system relies upon the ability to integrate a "donor plasmid" containing a shRNA expression construct, into an “acceptor” locus through transient expression of Cre recombinase. Lowe discloses that this system is designed so that proper recombinants can be selected through reconstitution of the *hprt* gene. Lowe further discloses additionally, both the donor and acceptor constructs express coat color gene markers which can be used to score chimeric mice (p. 17, par [0172], lines 1-20). Lowe does not explicitly disclose a mouse comprising the shRNA luciferase/hprt expression vector with a luciferase repression phenotype. However, Lowe does teach the ES cell harboring and expressing the luciferase shRNA have suppressed luciferase expression and suggests that the ES cells are intended for producing mice with shRNA suppression of targeted genes. Although Lowe does not make the mouse, the mouse is clearly contemplated and it was well within the skill of the ordinary artisan at the time of filing to make the mouse envisioned and discussed by Lowe. Therefore, from the teachings of Lowe, an artisan of ordinary skill at the time of the invention would be able to produce a mouse comprising an expression vector comprising a shRNA construct that integrates into a polymerase II dependent locus and results in suppression of expression of a gene targeted by said shRNA with a reason expectation of success. Also, since an artisan of ordinary skill would have a reasonable expectation of obtaining the claimed mouse from the teachings of Lowe, an artisan would also be able to obtain tissues and cells from said mouse as is encompassed by claim 47.

Thus, Lowe clearly anticipate and/or renders obvious the instant claims because Lowe discloses the limitations of the claim expression vector and claimed cell culture as well as suggest and teach the claimed mouse and tissues that result from said mouse.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MARCIA S. NOBLE whose telephone number is (571)272-5545. The examiner can normally be reached on M-F 9 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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